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contacting said chromosomal material with a high complexity nucleic acid probe wherein at least one component of the high complexity nucleic acid probe is targeted to a paracentromeric-specific nucleic acid segment, allowing said probe to bind to said targeted chromosomal material and detecting said bound probe, wherein bound probe is indicative of the presence of target chromosomal material.

REMARKS

Entry of the foregoing and further and favorable reconsideration of the subject application pursuant to and consistent with 37 C.F.R. §1.112 is respectfully requested

By the present amendment, claim 50 has been amended to incorporate the limitation that the claimed method is directed to staining targeted interphase chromosomal material. This limitation was inadvertently omitted from the claim when it was introduced in Applicants' amendment dated December 10, 1997. As noted at page 4 of that paper, support for this amendment may be found at least at page 121, lines 21-23 of the instant application, and at page 37, lines 5-8 of the earliest-filed parent of the instant application (U.S. Serial No. 06/819,314, filed January 16, 1986). No new matter has been added.

Turning now to the Official Action, claims 1 and 48-50 are rejected under 35 U.S.C. §103(a) as purportedly obvious over U.S. Patent 4,710,465 to Weissman et al., in view of Lichter et al. (*PNAS* 85:9664-9668, 1988) and either of U.S. Patent

5,487,970 to Rowley et al. or Drabkin et al. (*PNAS* 82:6980-6984, 1985). This rejection, to the extent that it applies to the claims as amended, is respectfully traversed.

The requirements of a *prima facie* case of obviousness are set forth in MPEP 2143:

> To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations.

In order for the presently claimed invention to be obvious over the method disclosed by Weissman, all of these limitations must be either taught or suggested, or the Examiner must point to knowledge generally available to those of ordinary skill in the art to supplement the disclosure of Weissman.

The Examiner concedes at least one difference between the disclosure of Weissman and that of the present application. At page 4 of the Official Action, the Examiner admits that "Weissman et al. . . . does not disclose interphase target assays nor specifically assaying directed to translocations in chromosomes 3 and/or 17. " The Examiner then attempts to point to knowledge generally available to those of ordinary skill in the art to supplement the disclosure of Weissman, citing Lichter et al. for the proposition that metaphase and interphase targets are equivalent, and

Drabkin et al. and Rowley et al. for their purported disclosure of chromosome 3 and 17 translocation targets, respectively.

Applicants maintain and reiterate their position that the Lichter et al publication is not properly cited as prior art against the present application. The present application claims benefit of two earlier-filed applications: Serial No. 06/937,793, filed December 4, 1986, and Serial No. 06/819,314, filed January 16, 1986. However, Lichter et al. was published in December 1988. Consequently, the Lichter et al. publication is not properly cited as prior art against the present claims.

The Examiner argues that the present claims do not find support in Applicants' two earliest priority applications, thus leaving Applicants with a priority date for the present claims no earlier than Applicant's priority application filed in July, 1989 (07/382,094). However, even if the Examiner were to hold that the present claims are entitled to a priority date no earlier than their application filed in March 1991 (07/670,242), the Rowley et al. Patent cited by the Examiner would not be prior art to the present claims. Rowley et al. issued from an application filed in June 1993 (08/080,255), which is a continuation-in-part of an application filed in December 1992 (07/991,244), which is in turn a continuation-in-part of an application filed in June, 1992 (07/900,689). Consequently the Examiner must concede that, even assuming that the disclosure relied upon by the Examiner may be found in their earliest priority application (a courtesy that he is unwilling to extend to the present Applicants), Rowley et al. is indisputably not prior art to the present claims. As a

result, Rowley et al. cannot cure the deficiencies of the combination of Weissman et al., Lichter et al. and Drabkin et al.. On this basis alone, the present rejection does not make out a *prima facie* case of obviousness, as the Examiner has not pointed to evidence of chromosome 17 translocation targets *in the knowledge generally available to those of ordinary skill in the art at the time the present invention was made.* Consequently, because the cited publications do not teach or suggest **all** of the limitations of the present claims, as required by 35 U.S.C. §103, withdrawal of this rejection is respectfully requested.

Further and favorable action in the form of a Notice of Allowance is believed to be next in order and such action is earnestly solicited.

In the event that there are any questions concerning this amendment, or the application in general, the Examiner is respectfully urged to telephone the undersigned so that prosecution of this application may be expedited.

Respectfully submitted,

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Date: August 25, 1999